CHOOSE BREZTRI™ AEROSPHERE® FOR ITS POWER TO REDUCE EXACERBATIONS IN COPD[1]

BREZTRI™ AEROSPHERE®
budesonide / glycopyrronium / formoterol fumarate dihydrate pressurized inhalation suspension

BREZTRI™ AEROSPHERE® is indicated for the long-term maintenance treatment to reduce exacerbations of chronic obstructive pulmonary disease (COPD) and treat airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema who are not adequately treated by a combination of an ICS/LABA or a combination of a LAMA/LABA.[1]

Budesonide (ICS), glycopyrronium (LAMA), and formoterol (LABA) in 1 pMDI device*

ICS = Inhaled corticosteroid; LABA = Long-acting beta$_2$-adrenergic agonist;
LAMA = Long-acting muscarinic antagonist; pMDI = Pressurized metered-dose inhaler.
* Clinical significance has not been established.

KEY FACTS ABOUT EXACERBATIONS IN COPD[2]

According to the CTS guidelines:

- **Exacerbations accelerate lung function decline**
- **Exacerbations dramatically reduce quality of life**

CHOOSE POWERFUL DEMONSTRATED EFFICACY AGAINST MODERATE TO SEVERE EXACERBATIONS (INCLUDING THOSE RESULTING IN COPD HOSPITALIZATIONS OR RISK OF DEATH)

KRONOS*

Reduction in rate of

MODERATE OR SEVERE EXACERBATIONS†

vs. a LAMA/LABA (GFF MDI)
0.46 vs. 0.95, respectively (HR: 0.48; 95% CI: 0.37, 0.64; $p<0.0001$; 2° endpoint)[1]

18% numerical reduction in rate of moderate or severe exacerbations vs. an ICS/LABA (BFF MDI; HR: 0.82; 95% CI: 0.58, 1.17; $p=0.2792$)[1,3]

ETHOS‡

Reduction in rate of

SEVERE EXACERBATIONS
(resulting in hospitalization or death)

vs. an ICS/LABA (BFF MDI)
0.13 vs. 0.16 respectively (HR: 0.80; 95% CI: 0.66, 0.97; $p=0.0221$)[1,4‡]

16% numerical reduction in rate of severe exacerbations vs. a LAMA/LABA (GFF MDI; HR: 0.84; 95% CI: 0.69, 1.03; $p=0.0944$)[1]

BFF = Budesonide and formoterol fumarate dihydrate; BGF = Budesonide/glycopyrronium/formoterol fumarate; GFF = Glycopyrronium/formoterol fumarate dihydrate; MDI = Metered dose inhaler.

* KRONOS: 24-week randomized, double-blind, multicentre, chronic-dosing, parallel-group study in 1,896 patients with moderate to very severe COPD with or without exacerbations in the year prior to screening. Patients were allocated BREZTRI™ AEROSPHERE® (364/16.4/11.6 mcg), GFF MDI (16.4/11.6 mcg), BFF MDI (364/11.6 mcg), or open-label budesonide/formoterol fumarate dihydrate dry powder for inhalation (400/12 mcg), all administered twice-daily. The two primary endpoints were FEV_1 area under the curve from 0-4 hours and change from baseline in morning pre-dose trough FEV_1 over 24 weeks.

† Moderate exacerbation was defined as: treatment with systemic corticosteroids and/or antibiotics for 3 or more days required. Severe exacerbation was defined as: resulting in hospitalization or death.

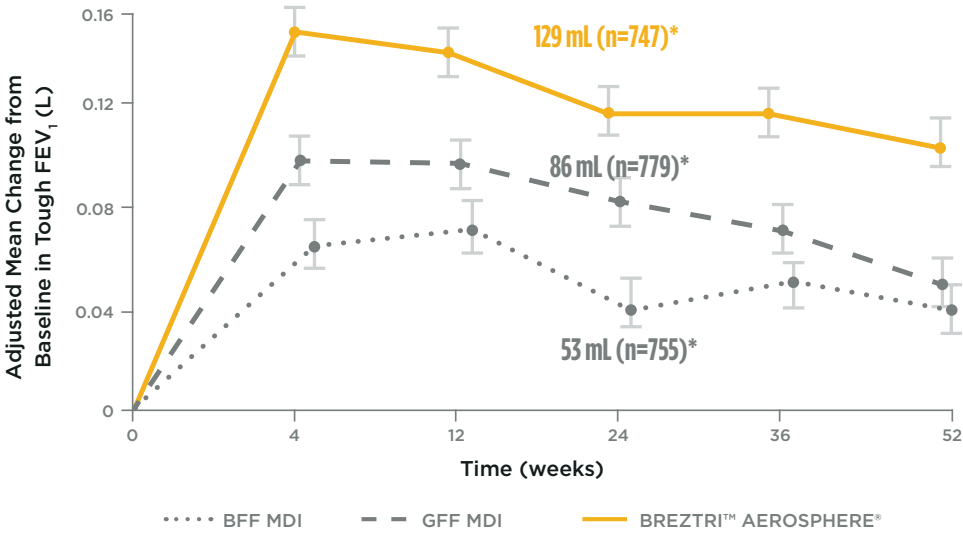
‡ ETHOS: 52-week randomized, double-blind, multicentre, parallel-group study in 8,509 patients with moderate to very severe COPD with a history of 1 or more moderate or severe COPD exacerbation(s) in the year prior to screening. Patients were allocated BREZTRI™ AEROSPHERE® (364/16.4/11.6 mcg), BGF MDI (182/16.4/11.6 mcg), GFF MDI (16.4/11.6 mcg), or BFF MDI (364/11.6 mcg), all administered twice-daily. The primary endpoint was the rate of moderate or severe COPD exacerbations.

ETHOS trial

POWERFUL AND SUSTAINED IMPROVEMENTS OBSERVED IN LUNG FUNCTION (FEV_1) OVER 24 WEEKS VS. A LAMA/LABA (GFF MDI) AND AN ICS/LABA (BFF MDI) (SUB-STUDY; 1° ENDPOINT)[1,5]

BREZTRI™ AEROSPHERE® provided statistically significant improvements in trough FEV_1 vs. a LAMA/LABA (GFF MDI) and an ICS/LABA (BFF MDI)

- The improvements in lung function were sustained up to 52-weeks



43 mL improvement vs. a LAMA/LABA (GFF MDI) (95% CI: 25, 60; *p*<0.0001)†

76 mL improvement vs. an ICS/LABA (BFF MDI) (95% CI: 58, 94; *p*<0.0001)

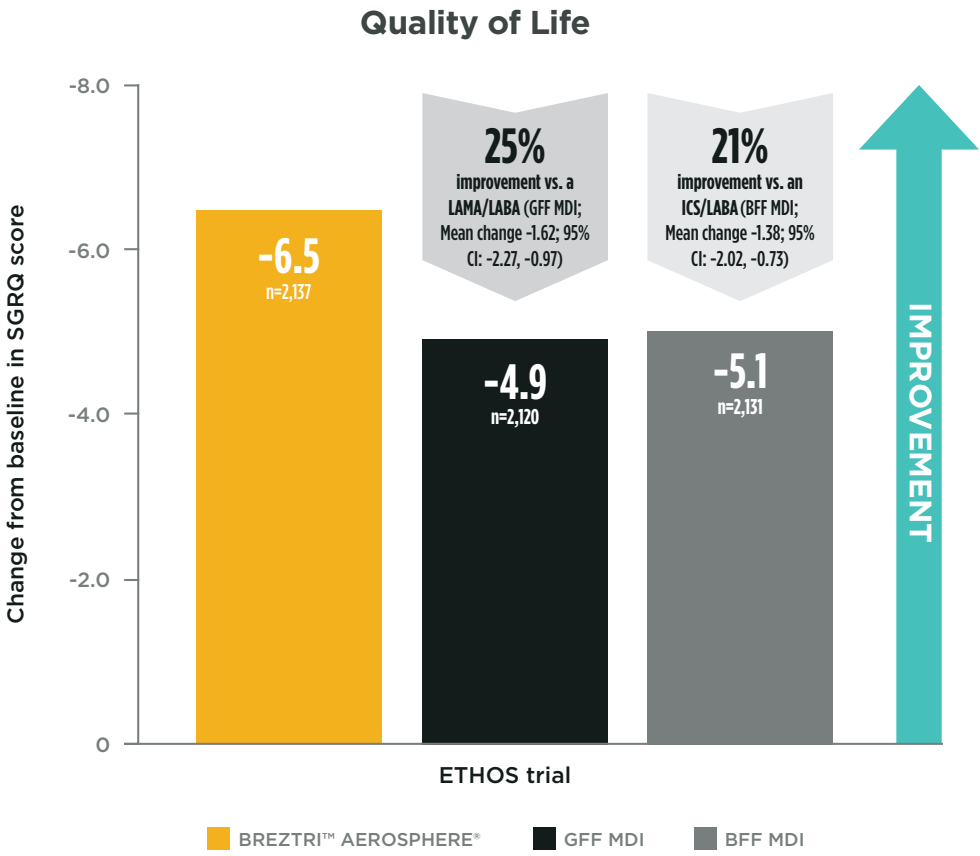
Adapted from the BREZTRI™ AEROSPHERE® Product Monograph and Data on File.[1,5]

	BREZTRI™ AEROSPHERE® (n=747)*	GFF MDI (n=779)*	BFF MDI (n=755)*
FEV_1 $AUC_{0\text{-}4}$ over 24 weeks, LS mean change from baseline (SE)	294 mL (6.3)	245 mL (6.3)	194 mL (6.3)
		49 mL improvement vs. a LAMA/LABA (GFF MDI) (95% CI: 31, 66; *p*<0.0001)	99 mL improvement vs. an ICS/LABA (BFF MDI) (95% CI: 82, 117; *p*<0.0001)†

* Administered orally as two inhalations of BREZTRI™ AEROSPHERE® 182/8.2/5.8 mcg, GFF MDI 8.2/5.8 mcg, BFF MDI 182/5.8 mcg, BID.
† Statistically significant.

POWERFUL IMPROVEMENTS IN QUALITY OF LIFE (SGRQ) (2° ENDPOINT)[1,3,4¶]

Statistically significant improvements in patient quality of life were observed over 24 weeks vs. a LAMA/LABA (GFF MDI) and vs. an ICS/LABA (BFF MDI) in the ETHOS trial.[1]



Adapted from the BREZTRI™ AEROSPHERE® Product Monograph, Rabe *et al.* (suppl.) and Ferguson *et al.*

36% increase in likelihood of clinically important improvement in SGRQ for BREZTRI™ AEROSPHERE® vs. a LAMA/LABA (GFF MDI) at week 24 (OR: 1.358; 95% CI: 1.199, 1.539; $p<0.0001$).[6]**

A ≥4-unit change in the SGRQ score is clinically important.[7]

MCID = Minimal clinically important difference; SGRQ = St. George's Respiratory Questionnaire.
¶ Quality of life assessed by the SGRQ score.
** Clinically important improvement defined as achieving an MCID decrease of ≥4 units.[9]

CHOOSE BREZTRI™ AEROSPHERE® FOR YOUR COPD PATIENTS: DEMONSTRATED POWERFUL EFFICACY AND SAFETY

BREZTRI™ AEROSPHERE® offers:

Demonstrated reduction in moderate and severe COPD exacerbations, regardless of patients' recent exacerbation history[1]

Significant improvements observed in quality of life and breathlessness

Demonstrated consistent safety profile with the known pharmacologic class effects of ICSs, LAMAs and/or LABAs[1]

Clinical use:

BREZTRI™ AEROSPHERE® is not indicated for:

- Treatment of acute episodes of bronchospasm or asthma.
- Use in pediatric patients <18 years of age.

Relevant warnings & precautions:

- Risk of serious asthma-related events, including hospitalization, intubations, and death
- Should not be used in patients with deteriorating COPD
- Excessive use with other LAMA and LABA products
- Anticholinergic activity: use with caution in patients with symptomatic prostatic hyperplasia, urinary retention or narrow-angle glaucoma
- Cardiovascular effects, including arrythmias and changes in pulse and blood pressure, QTc prolongation
- Driving and operating machinery
- Candidiasis
- Risk of systemic effects, including Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, hypokalemia and hyperglycemia, cataract, intraocular pressure, and glaucoma
- Hypercorticism, adrenal suppression
- Adrenal insufficiency in patients transferred from systemic steroid
- Patients with symptomatic prostatic hyperplasia, glaucoma, convulsive disorders, thyrotoxicosis, sensitivity to sympathomimetic amines, severe hepatic impairment/hepatic disease, or urinary retention
- In rare cases, eosinophilic conditions
- Susceptibility or decreased resistance to infections
- Monitoring of hypokalemia, hyperglycemia, bone and ocular effects, and corticosteroid effects in patients with hepatic impairment
- Paradoxical bronchospasm
- Increased risk of pneumonia
- Pregnant and nursing women
- Geriatrics (≥65 years of age)

For more information:

Consult the Product Monograph at breztri-en.azpm.ca for important information regarding adverse reactions, drug interactions and dosing. The Product Monograph is also available by calling AstraZeneca Canada at **1-800-668-6000.**

References: 1. BREZTRI™ AEROSPHERE® Product Monograph. AstraZeneca Canada Inc., September 30, 2021. **2.** Bourbeau J, *et al*. Available at: https://cts-sct.ca/wp-content/uploads/2019/10/CTS-COPD-Rx-2019-Guideline_Final.pdf. **3.** Ferguson GT, *et al. Lancet*. 2018;6(10):747–758. **4.** Rabe KF, *et al. NEJM*. 2020;383:35–48 (inc. supplement). **5.** Data on file – ETHOS trial Table 2.14.1. AstraZeneca Canada Inc. **6.** Martinez FJ, *et al. Respir Med*. 2021;185:106509. **7.** Food and Drug Administration. Available at: https://www.fda.gov/files/drugs/published/Chronic-Obstructive-Pulmonary-Disease-Use-of-the-St.-George's-Respiratory-Questionnaire-as-a-PRO-Assessment-Tool-Guidance-for-Industry.pdf.

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AstraZeneca

CA-5949

REVIEWED BY PAAB